

MANTZARIDIS et al
Serial No. 09/973,568
Amendment in RCE dated November 21, 2003
Reply to Office Action dated May 21, 2003

REMARKS

Upon entry of this amendment, claims 1-4, 7-18 and 20-33 are pending. By the present amendment, claims 1 and 9 have been amended for clarity and new claims 20-33 have been added. Favorable reconsideration of the application is respectfully requested.

The objection to claim 1 is respectfully traversed. Without acquiescing in the objection, claim 1 has been amended for clarity and to overcome the objection. Accordingly, reconsideration and withdrawal of the objection are respectfully requested.

The rejection of claims 1-4, 7, 9 and 11-18 under 35 U.S.C. §103(a) over John (U.S. Patent No. 6,067,467) in view of Webb et al. "Closed-loop control of depth of anaesthesia" (hereinafter Webb), and further in view of DeBeer et al. (British Journal of Anaesthesia, pp. 685-693, May, 1996, hereinafter "DeBeer") is respectfully traversed. Without acquiescing in the rejection, claims 1 and 9 have been amended for clarity. Accordingly, the rejection will be discussed with respect to the amended and pending claims.

John is directed to an electroencephalograph (EEG) method to monitor patients during and after medical operations. According to John, an anesthesiologist administers sufficient anesthetics to cause the patient to attain a desired plane of anesthesia. The patient's brain waves, both ongoing and evoked by stimuli are amplified, digitized and recorded. The pre-operative set of brain wave data is compared to a set of the patient's brain wave data obtained during the operation in order to determine if additional, or less,

anesthesia is required, paying particular attention to the relative power in the theta band, as an indication of brain blood flow, and prolongations of the latency periods under brain stem stimuli, as an indication of the patient's ability to feel pain. A *set* of neurometric features are extracted, converted into a normalized statistical score, a discriminant score is thereby developed and the discriminant score is converted into a patient state index using probability functions.

John does not teach or suggest the calculation of an index relating to the depth of anesthesia based upon the coarseness of the measured signal as a *single* measured value, as specifically set forth in the claims. Instead, John presents a complex method based on the statistical analysis and weighting of a number of EEG parameters. According to John, each parameter is assigned a score that is calculated from the differences of pre-operative and intra-operative measurements that are weighted and summed to give two numerical measures for state while the patient is (1) awake; and (2) unconscious. The weighting used for these two states differ and are based on "experience and experimentation" (see, e.g., Col. 10, lines 21-22). From the resulting measures, the probability of the patient being awake or unconscious is calculated (see, e.g., Col. 10, lines 30-40). Moreover, John requires each of the measured parameters to be measured with reference to a previous measurement of that parameter while the patient was in a known anaesthetized state (*e.g.*, the "first set of data" and the "second set of data" in John).

Webb is directed to improving the use of neural networks in analyzing and evaluating AEP signals for use in an anesthetic control system. Webb does not disclose, teach or suggest calculation of an index relating to the depth of anesthesia based upon the coarseness of the measured AEP signal, as specifically set forth in the claims. Moreover, the combination of Webb with John would at best result in a system in which numerous measures, perhaps even including an AEP signal, are used in a complex statistical analysis in an effort to determine a probability of a patient being awake

DeBeer is directed to determining haemodynamic responses to incision and sternotomy in relation to AEP, and does *not* relate to measuring a depth of anaesthesia related to awareness. At best, it is only suggested in the summary of DeBeer that AEP might at some future time be used to help in predicting inadequate anesthesia. However, this is not by any means a specific teaching of using AEP in the manner claimed to provide a measure of anaesthetic depth. The examples set forth in DeBeer are only related to haemodynamic responses and *not* consciousness. Moreover, the conclusion of DeBeer is that "the feasibility of routine AEP and EEG monitoring in the operating theatre is *questionable* at present." Emphasis added (see, *e.g.*, page 692, column 2, last paragraph). This conclusion teaches directly away from the specifically claimed invention.

The three-way combination set forth in the Office Action fails to even establish a *prima facie* case of obviousness. For example, there is no teaching or suggestion

anywhere in any of the cited references of the specifically claimed feature of providing a signal corresponding to the coarseness of the monitored AEP signal, *the coarseness of the signal being a single measure increasing with both amplitude and frequency of variations in the AEP signal and using said signal as said index indicative of anaesthetic depth*. At best, the disparate teachings of the varied references, in combination, only consider measuring a large number of attributes of the raw AEP and other EEG signals, and hoping that by statistical analysis they can derive a combination of these numerous measurements to arrive at something that might be clinically useful.

In complete contrast and distinction, the specifically claimed features enumerated above are unique among all of the other measures that have been tried in the cited prior art in that it can, *by itself*, provide a sufficiently reliable indicator of consciousness, without the need to combine it with other measures of confidence. This use of a single measure is directly contrary to the teachings in the prior art. None of the prior art cited in the Office Action holds out any hope that such a measure can be found, even if they might remotely suggest that AEP may have some value as part of a much more elaborate statistical combination measure.

Instead, and in stark contrast, John presents a complex statistical analysis and weighting of a wide variety of different EEG parameters to arrive at his depth of anesthesia determination. The claimed method is completely distinct from the complex multi-variable approach of John in that the claimed invention analyzes the morphology of

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one signal, i.e., the coarseness of AEP, to calculate an index indicative of anesthetic depth. As discussed above, Webb and DeBeer simply fail to overcome this fundamental deficiency of John.

Simply stated, there is no teaching or suggestion in John, Webb or DeBeer of calculating an index relating to the depth of anesthesia based on the coarseness of the AEP signal as claimed. Even if, *arguendo*, the combination of John, Webb and DeBeer were proper, the combination would, at best, result in a system in which AEP measures are merely minor components that are used in a complex statistical analysis of numerous other measures in an effort to determine a probability of a patient being awake. Moreover, the combination even when made fails to disclose or suggest using the coarseness of the AEP signal as set forth in the claims. Accordingly, the combination of John, Webb and DeBeer fails to render the claimed invention obvious. Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

The rejection of claims 8 and 10 under 35 U.S.C. §103(a) over John '467 in view of Webb and DeBeer and further in view of Cosgrove, Jr. et al. (U.S. Patent No. 4,280,494, hereinafter "Cosgrove") is respectfully traversed.

It is respectfully submitted that Cosgrove fails to overcome the fundamental deficiencies noted above with respect to John, Webb and DeBeer. Therefore, even if, *arguendo*, the combination of Cosgrove, John, Webb and DeBeer were proper, the

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combination nevertheless fails to render the claimed invention obvious. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

In view of the foregoing, it is respectfully submitted that the entire application is in condition for allowance. Favorable reconsideration of the application and prompt allowance of the claims are earnestly solicited.

Should the Examiner deem that further issues require resolution prior to allowance, the Examiner is invited to contact the undersigned attorney of record at the telephone number set forth below.

Respectfully submitted,
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